REMARKS

Claims 1-5, 7-10, and 12-18 are pending in the instant application. Claim 11 has been canceled. Claims 19 and 20 have been added. Claims 1-4 and 10-18 have been rejected. Claims 5 and 7-9 have been objected to. The Examiner has made this Office Action FINAL.

Newly submitted claims 19 and 20 find support on page 14 of the specification and in claim 5. These claims do not add new subject matter to the application. Accordingly, applicants respectfully requests consideration and entry of these amendments.

Please note that the patent attorney handling this application is Hal Brent Woodrow, who is included under Customer Number 000027777. Consequently the correspondence address remains the same. Mr. Woodrow may be contacted by phone at 732-524-2976.

Reconsideration of the captioned application based on the previous amendments and following remarks is respectfully requested.

Applicants respectfully requests reconsideration and withdrawal of the finality of the last Office Action. In the last Office Action a new rejection of Claims 1-4 and 10-18 under 35 U.S.C. §112, first paragraph, was made:

> "because the specification is only enabling for using the compound of claims 5,7-9 for treating emesis, pain, depression or anxiety. The specification does not enable any person skilled in the art to which it pertains, or with which it is most connected, to use the invention commensurate in scope with these claims."

Applicants submit that this is the ***first*** time that the Examiner has made this rejection and that the rejection was not necessitated by the applicant's previous amendment nor is the rejection based on a new reference. As such it is improper to make the current Office Action Final at this time. **(MPEP 706.07(a))** Applicants, therefore, respectfully request that the finality of the last Office Action be reconsidered and withdrawn.

The Examiner has maintained the objection to Claim 11 as being a substantial duplicate of claim 10.

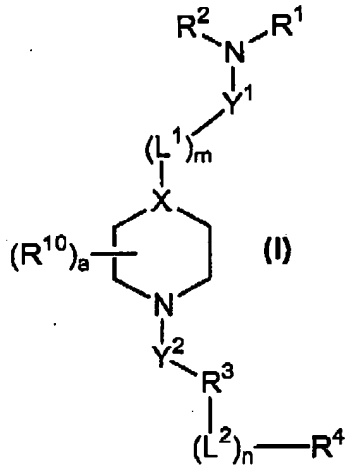
Applicants respectfully traverse this rejection. Applicants maintain that Claims 10 and 11 are not substantial duplicates, as they are directed to a pharmaceutical composition and a product by process composition, respectfully. The claims are not substantial duplicate claims, as they are not so close in content that they cover the same thing/invention.

Applicants further submit that "'claims may be multiplied ... to define the metes and bounds of the invention in a variety of ways.' Thus two claims that read differently can cover the same subject matter." *Tanden Corp. v. United States Internation Trade Commission,* 831 F.2d 1017, 4 U.S.P.Q.2d 1283 (Fed. Cir. 1987)

To expedite prosecution, Applicants have canceled claim 11.

The Examiner has maintained the rejection of Claims 1-4 and 10-12 under 35 U.S.C. §103(a) as unpatentable over Himmelsbach et al., (USPN 5,736,559).

Applicants respectfully traverse the rejection for the reasons previously presented. Applicants maintain that the instant application is directed to compounds of formula (I)



(I)

i.e. substituted piperidinyl derivatives wherein X is CH or $C(C_{1-6}alkyl)$, wherein the 4-position of the piperidinyl core is substituted with an aminocarbonyl- or aminocarbonyl-alkyl- group (or an aminothiocarbonyl or aminothiocarbonyl-alkyl- group) of the formula $-(L^1)_m-Y^1-N(R^1R^2)$, and wherein the 1-position of the piperidinyl core is substituted with a group of the formula $-Y^2-R^3-(L^2)_n-R^4$ wherein R^3 and R^4 are both required to be ring groups.

Himmelsbach et al., discloses biphenyl derivatives, including more than 300 specific compounds. Of the more than 300 exemplified compounds, only 85 contain a substituted piperidinyl group, the majority of which are further substituted at the 4-position of the piperidine with an alkoxycarbonyl-alkyl- group.

Only two of the more than 300 exemplified compounds are drawn to biphenyl derivatives containing a piperidinyl group, wherein the piperidinyl is substituted at the 4-position with an aminocarbonyl- or aminocarbonyl-alkyl- substituted piperidinyl (compound #82, column 27 and compound #6, column 34).

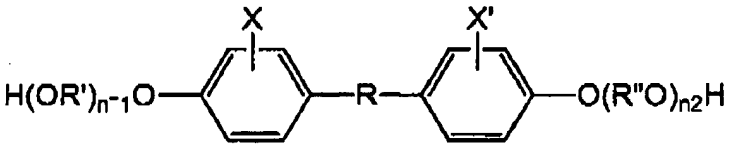
Additionally, Himmelsbach et al., does not claim 1-biphenyl-carbonyl-, 4-aminocarbonyl- or 4-aminocarbonyl-alkyl- substituted piperidinyl compounds. Clearly, the teaching of Himmelsbach et al., would not motivate one of ordinary skill in the art to make the aminocarbonyl- or aminocarbonyl-alkyl-piperidine compounds claimed in the instant application.

Applicants additionally submit that there is nothing in Himmelsbach et al., which would suggest the desirability of the substituted piperidinyl derivatives of the instant application. Applicants submit that the generic disclosure of biphenyl derivatives in Himmelsbach et al., contains a large number of variables (i.e. X, A, B, C, D and E) which requires picking and choosing "some" substituents from among the "many" to yield the compounds of the instant application. Further, Applicants submit that there is nothing in the reference disclosure suggesting the preparation of substituted piperidinyl derivatives. Indeed, the reference appears to teach away from the substituted piperidinyl derivatives by focusing on and only claiming biphenyl derivatives. Applicants therefore maintain that the reference does not provide the requisite motivation for the selection of the appropriate variables required to yield the substituted piperidinyl derivatives of the instant application. *In re Baird*, 16 F.3d 380, 29 U.S.P.Q.2d 1550, 1552 (Fed. Cir. 1994)

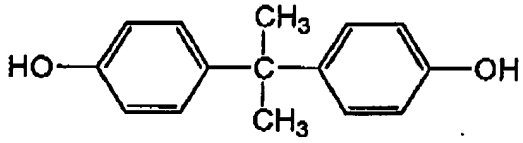
Applicants respectfully refer the Examiner to the Federal Circuit Decision *In re Baird*, 16 F.3d 380, 29 U.S.P.Q.2d 1550, 1552 (Fed. Cir. 1994), which is briefly summarized and discussed below.

Baird claimed a flash fusable toner comprising a binder resin which is a bisphenol A polyester containing an aliphatic di[carboxylic] acid selected form the group consisting of succinic acid, glutaric acid and adipic acid.

Knapp et al., in US Patent No 4,634,649 disclosed developer compositions comprised of, *inter alia*, the polymeric esterification product of a dicarboxylic acid and a diphenol of the generic formula



wherein the variables R, R', R', X, X' and n contained a broad range of variables and thus encompassed a large number of different diphenols, including bisphenol A, shown in Baird's application as having the following structure

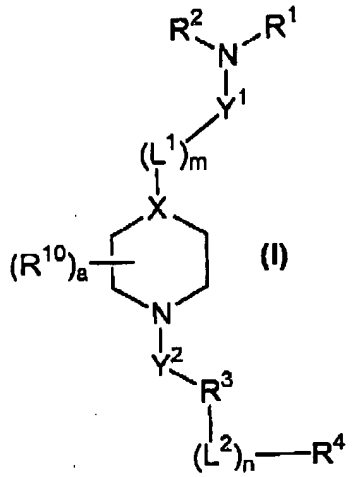


Knapp et al., also discloses that the dicarboxylic acids have the general formula HOOCR"'n3COOH. Twenty typical discarboxylic acids were recited by Knapp et al., including succinic acid, glutaric acid and adipic acid.

Recognizing that bisphenol A is defined when certain specific variables are chosen, the Examiner reasoned that bisphenol A "may be easily derived from the generic formula of the diphenol in [Knapp] and all the motivation the worker of ordinary skill in the art needs to arrive at the particular polyester of the instant claim [] is to follow [that formula]. The Board upheld the Examiner's rejection.

The question before the Federal Circuit was whether the record supported the Board's conclusion that, in view of the teachings of Knapp et al., the claimed compounds would have been obvious to one of ordinary skill in the art. *Baird argued that there was no suggestion in Knapp et al. to select bisphenol A from the vast number of biphenols covered by the generic formula disclosed by Knapp et al.* The Federal Circuit concluded that "while the Knapp formula unquestionably encompasses bisphenol A when specific variables are chosen, there is nothing in the disclosure of Knapp suggesting that one should select such variables. Indeed, Knapp appears to teach away from the selection of bisphenol A by focusing on more complex diphenols..."

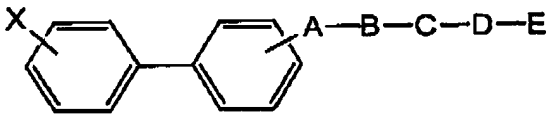
In the instant application, Applicants claim compounds of the general formula (I)



(I)

i.e. substituted piperidinyl derivatives wherein X is CH or $C(C_{1-6}alkyl)$, wherein the 4-position of the piperidinyl core is substituted with an aminocarbonyl- or aminocarbonyl-alkyl- group (or an aminothiocarbonyl or aminothiocarbonyl-alkyl- group) of the formula $-(L^1)_m-Y^1-N(R^1R^2)$, and wherein the 1-position of the piperidinyl core is substituted with a group of the formula $-Y^2-R^3-(L^2)_n-R^4$ wherein R^3 and R^4 are both required to be ring groups.

Himmelsbach et al., discloses biphenyl derivatives of the general formula



wherein X, A, B, C, D and E are defined as encompassing a broad range of substituent groups. As in Baird, the genus of Himmelsbach et al., would encompass some of the compounds of the present invention, if specific substituents for the variables were chosen. However, as in Baird, there is no suggestion within the disclosure of Himmelsbach et al., to select the specific substituents which would result in the substituted piperidinyl

compounds of the instant invention. Further, as in Baird, the teachings in Himmelsbach et al., teach away from the compounds of the present invention, by focusing on complex biphenyl derivatives wherein, the biphenyl ring is bound to a 4-substituted piperidinyl group, wherein the 4-position is not aminocarbonyl or aminocarbonyl-alkyl, as in the compounds of the present invention (i.e. not a substituent of the formula R^1R^2N-Y^1-$((L^1)_m$- as in the compounds of formula (I) of the instant invention.).

Thus, Applicants urge that the teaching of Himmelsbach does not render the present invention obvious and Applicants respectfully request that the Examiner withdraw the rejection of Claims 1-4 and 10-12 under 35 U.S.C. §103(a).

The Examiner has maintained the rejection of Claims 1-3 and 10-15 under 35 U.S.C. §103(a) as unpatentable over Sugimoto et al., (USPN 4,895,841).

Applicants respectfully traverse the rejection. As discussed in detail above, the instant invention is directed to substituted piperidinyl derivatives wherein the 4-position of the piperidinyl core is substituted with an aminocarbonyl- or aminocarbonyl-alkyl- group (or an aminothiocarbonyl or aminothiocarbonyl-alkyl- group) of the formula $-(L^1)_m$-Y^1-$N(R^1R^2)$, and wherein the 1-position of the piperidinyl core is substituted with a group of the formula $-Y^3$-R^3-$(L^2)_n$-R^4 wherein R^3 and R^4 are both required to be ring groups.

Applicants submit that Sugimoto et al., discloses substituted piperidinyl compounds, including 249 specific examples. However,

of the specific examples in Sugimoto et al., only four compounds (Examples 20, in column 43 and Examples 48, 49, 50 in column 55) are substituted piperidinyl compounds wherein the 4-position is substituted with an aminocarbonyl-alkyl- substituent. These four compounds are substituted at the 1-position of the piperidinyl with a benzyl or phenyl-carbonyl substituent, rather than with a substituent containing two ring groups (i.e., a group of the formula $-Y^2-R^3-(L^2)_n-R^4$) as required in the compounds of the instant invention. Further, more than half of the specific examples disclosed by Sugimoto et al., (138 compounds) are compounds wherein the 4-position of the piperidine is substituted with an optionally cyclic, reverse amide, i.e. with a substituted carbonyl-amino-alkyl- group (*see, e.g.*, Example 5 & 6 in columns 34-35, Example 14 & 15 in column 40 and others).

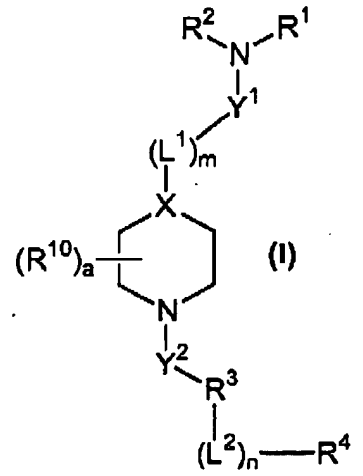
Additionally, of the specific examples in Sugimoto et al., only one compound of the 249 exemplified species (Example #237 in column 107-108) is a substituted piperidinyl compound wherein the substituent at the 1-position contains two ring groups. However, this compound does not have an aminocarbonyl- or aminocarbonyl-alkyl- substituent on the 4-position of the piperidine.

Applicants therefore maintain that the teaching of Sugimoto et al., would not motivate one of ordinary skill in the art to make the compounds of the instant invention, i.e. substituted piperidinyl derivatives wherein the piperidinyl core is substituted at the 4-position with an aminocarbonyl or aminocarbonyl-alkyl group and wherein the 1-position is substituted with a substituent group of the formula $-Y^2-R^3-(L^2)_n-R^4$.

Applicants additionally submit that there is nothing in Sugimoto et al., which would suggest the desirability of the substituted piperidinyl derivatives of the instant application. Applicants submit that the generic disclosure of cyclic amine compounds in Sugimoto et al., contains a large number of variables (i.e. J, B, T, q, Q and K) which requires picking and choosing "some" substituents from among the "many" to yield the compounds of the instant application. Further, Applicants submit that there is nothing in the reference disclosure suggesting the preparation or desirability of substituted piperidinyl derivatives wherein the 4-position is substitiuted with an aminocarbonyl or aminocarbonyl-alkyl group and the 1-position is substituted with a group of the formula $-Y^2-R^3-(L^2)_n-R^4$ wherein R^3 and R^4 are both required to be ring groups. Indeed, the reference appears to teach away from such substituted piperidinyl derivatives by focusing on substituted piperidinyl derivatives wherein the 1-position is substituted with a group containing only one ring group.

Applicants therefore maintain that the reference does not provide the requisite motivation for the selection of the appropriate variables required to yield the substituted piperidinyl derivatives of the instant application. *In re Baird*, 16 F.3d 380, 29 U.S.P.Q.2d 1550, 1552 (Fed. Cir. 1994)

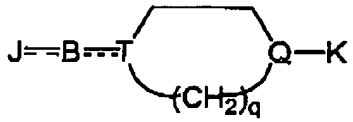
In the instant application, Applicants claim compounds of the general formula (I)



(I)

i.e. substituted piperidinyl derivatives wherein X is CH or $C(C_{1-6}alkyl)$, wherein the 4-position of the piperidinyl core is substituted with an aminocarbonyl- or aminocarbonyl-alkyl- group (or an aminothiocarbonyl or aminothiocarbonyl-alkyl- group) of the formula $-(L^1)_m-Y^1-N(R^1R^2)$, and wherein the 1-position of the piperidinyl core is substituted with a group of the formula $-Y^2-R^3-(L^2)_n-R^4$ wherein R^3 and R^4 are both required to be ring groups.

Sugimoto et al., disclose cyclic amine compounds of the general formula



wherein J, B, T, q, Q and K are defined as encompassing a broad range of substituent groups. As in Baird, the genus of Sugimoto et al., would encompass some of the compounds of the present invention, if specific substituents for the variables were chosen. However, as in Baird, there is no suggestion within the disclosure of Sugimoto et al., to select the specific substituents which would result in the 4-aminocarbonyl- or 4-aminocarbonyl-alkyl-piperidinyl derivatives substituted at the 1-position with a

group of the formula $-Y^2-R^3-(L^2)_n-R^4$ wherein R^3 and R^4 are both required to be ring groups, the compounds of the instant invention. Further, as in Baird, the teachings in Sugimoto et al., teach away from the compounds of the present invention, by focusing on complex substituted piperidinyl compounds wherein the 1-position of the piperidinyl is substituted with a single ring and wherein the 4-position is substituted with a complex ring structure, not with a group of the formula $-(L^1)_m-Y^1-N(R^1R^2)$, as required in the compounds of the instant invention.

Thus, Applicants submit that the teaching of Sugimoto et al., does not render the present invention obvious and Applicants respectfully request that the Examiner withdraw the rejection of Claims 1-3 and 10-15 under 35 U.S.C. §103(a).

With respect to the rejection of Claims 1-4 and 10-18 under 35 U.S.C. §112, Applicants respectfully traverse the rejection. Applicants submit that claims 1-4 are directed to compounds of formula (I). Claims 10 and 12 are directed to a pharmaceutical composition, and a process for the preparation of the pharmaceutical compositions, respectively. Claims 13 and 14 are directed to methods for the treatment of nervous system disorders.

Applicants submit that the specification as filed adequately teaches one of ordinary skill in the art how to make and use the claimed compounds. Methods of making the genus claimed compounds are provided on pages 21 through 61 and 66 through 102. With respect to the adequacy of disclosure that a claimed genus possess an asserted utility, the disclosure of representative examples

together with a statement applicable to the genus as a whole will ordinarily be sufficient if it would be deemed likely by one skilled in the art that the claimed genus would possess the asserted utility. The specification clearly discloses use of the instant compounds for these utilities (*see, e.g.*, page 9, line 28 through page 10, line 32; page 20, line 13 through page 21, line 6, page 61, lines 5-12). Moreover, page 61, line 14 through page 62, line 27 and page 63, line 20 through page 66, line 6 of the specification teaches pharmaceutical compositions of the claimed compounds, methods for the preparation of said pharmaceutical compositions and how the compounds and / or pharmaceutical compositions may be used (e.g., route of administration, dosages) to treat nervous system disorders. Thus, Applicants urge that the instant specification provides a teaching of how to use the invention, which would be credible to the skilled artisan, and moreover, that one of ordinary skill in the art would be able to use the compounds for the stated utility without undue experimentation.

Moreover, an Applicant's assertion of utility creates a presumption of utility and the Examiner has the initial burden of challenging a presumptively correct assertion of utility in the disclosure; only after the Examiner provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility. Applicants maintain that the Examiner has not provided evidence that would cause the skilled artisan to doubt Applicants' teachings of utility which are set forth in detail above. Therefore, Applicants maintain that the

Examiner has failed to establish a *prima facie* case that the claimed invention lacks utility.

Applicants further submit that representative compounds of the instant invention have been tested *in vitro* for inhibition of the Neurokinin-1 (NK-1) and Neurokinin-2 (NK-2) receptor activity, substantially in according to the procedures in Exhibit A and B, and with results in Exhibit C, attached hereto. A declaration under 37 C.F.R. Rule 1.132 will be submitted hereinafter in support of these procedures and results. Applicants, therefore, respectfully requests consideration of this data.

Applicants therefore respectfully request that the Examiner withdraw the rejection of Claims 1-4 and 10-14 under 35 U.S.C. 112, first paragraph.

The Examiner has objected to Claims 5, 7-9 and 16-18 as being dependent upon a rejected base claims. Applicants acknowledges the allowability of these claims, and respectfully requests the Examiner allow claims 1-4, 10 and 12-15 in view of the arguments presented above and withdraw the objection to claims 5, 7-9 and 16-18.

In view of the above remarks, Applicants maintain that the application is in condition for allowance and passage to issue is earnestly requested.

Respectfully submitted,

Hal Woodrow
Attorney for Applicants
Reg. No. 32,501

Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003
(732) 524-2976
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